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EFFECT OF APIXABAN, AN ORAL, DIRECT AND SELECTIVE FACTOR XA INHIBITOR ON INFLAMMATORY BIOMARKERS FOLLOWING ACUTE CORONARY SYNDROME

ACC Poster Contributions
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Background: Apixaban is an oral, direct and selective factor Xa inhibitor under development for secondary prevention in acute coronary syndrome (ACS).

Methods: Apixaban's effect on biomarkers of inflammation and coagulant regulatory proteins was assessed in a randomized, double-blinded, placebo-controlled phase 2 dose-ranging trial. Samples were obtained at baseline , week 3 and week 26 in 1715 patients with ST-segment elevation or non-ST elevation ACS who received apixaban (5-20mg daily) or placebo. Apixaban plasma concentrations were measured directly by LC/MS/MS, and anti-Xa activity was determined with a chromogenic assay using an apixaban calibrator.

Results: There was a strong, direct and linear relationship between apixaban plasma concentration and anti-Xa activity (r= 0.97). High sensitivity (hs) C-reactive protein (CRP) ($p<0.0001$) fibrinogen, ($p<0.0001$), soluble CD-40Ligand (sCD40L) ($p<0.0001$) and myeloperoxidase (MPO) ($p=0.00001$) decreased over time from elevated baseline values in all groups. Tissue factor pathway inhibitor (TFPI) increased over time ($p<0.0001$). The changes were greater at week 26 compared with week 3 across increasing quartiles of apixaban plasma concentration and anti-Xa activity(figure).An apixaban level between 100 and 200ng/ml, achieved with the 10mg total daily doses investigated in APPRAISE-2, AVEROES, and ARISTOTLE was associated with maximal suppression of hs-CRP ($p=0.03$), CD40L ($p=0.01$) and MPO ($p=0.04$) at 26 weeks of treatment.

Conclusions: Apixaban - an oral, direct and selective factor Xa inhibitor, in addition to its predicted anticoagulant effects may also attenuate leukocyte-and platelet-mediated inflammation and upregulate intrinsic anticoagulant activity, supporting the pleotropic properties of factor Xa.